

-141-

(DES), leuprolide, flutamide, cyproterone acetate, ketoconazole and amino glutethimide are preferred.

Immunotherapy

5 The cyclooxygenase-2 inhibitors of the present invention may also be used in combination with monoclonal antibodies in treating cancer. For example monoclonal antibodies may be used in treating prostate cancer. A specific example of such an antibody includes
10 cell membrane-specific anti-prostate antibody.

The present invention may also be used with immunotherapies based on polyclonal or monoclonal antibody-derived reagents, for instance. Monoclonal antibody-based reagents are most preferred in this
15 regard. Such reagents are well known to persons of ordinary skill in the art. Radiolabelled monoclonal antibodies for cancer therapy, such as the recently approved use of monoclonal antibody conjugated with strontium-89, also are well known to persons of ordinary
20 skill in the art.

Antiangiogenic Therapy

The cyclooxygenase inhibitors of the present invention may also be used in combination with other cyclooxygenase-2 inhibitors or other antiangiogenic agents in treating cancer. Antiangiogenic agents include
25 but are not limited to MMP inhibitors, integrin antagonists, COX-2 inhibitors, angiostatin, endostatin, thrombospondin-1, and interferon alpha. Examples of
30 preferred antiangiogenic agents include, but are not limited to vitaxin, marimastat, Bay-12-9566, AG-3340,

-142-

metastat, celecoxib, rofecoxib, JTE-522, EMD-121974, and D-2163 (BMS-275291).

Cryotherapy

5 Cryotherapy recently has been applied to the treatment of some cancers. Methods and compositions of the present invention also could be used in conjunction with an effective therapy of this type.

10 All of the various cell types of the body can be transformed into benign or malignant neoplasia or tumor cells and are contemplated as objects of the invention. A "benign" tumor cell denotes the non-invasive and non-metastasized state of a neoplasm. In man the most frequent neoplasia site is lung, followed by colorectal, 15 breast, prostate, bladder, pancreas, and then ovary. Other prevalent types of cancer include leukemia, central nervous system cancers, including brain cancer, melanoma, lymphoma, erythroleukemia, uterine cancer, and head and neck cancer. Examples 1 through 9 are provided 20 to illustrate contemplated therapeutic combinations, and are not intended to limit the scope of the invention.

Illustrations

25 The following non-limiting illustrative examples describe various cancer diseases and therapeutic approaches that may be used in the present invention, and are for illustrative purposes only. Preferred COX-2 inhibitors of the below non-limiting illustrations 30 include but are not limited to celecoxib, rofecoxib, and JTE-522.

-143-

Example 1

Lung Cancer

In many countries including Japan, Europe and America, the number of patients with lung cancer is fairly large and continues to increase year after year and is the most frequent cause of cancer death in both men and women. Although there are many potential causes for lung cancer, tobacco use, and particularly cigarette smoking, is the most important. Additionally, etiologic factors such as exposure to asbestos, especially in smokers, or radon are contributory factors. Also occupational hazards such as exposure to uranium have been identified as an important factor. Finally, genetic factors have also been identified as another factor that increase the risk of cancer.

Lung cancers can be histologically classified into non-small cell lung cancers (e.g. squamous cell carcinoma (epidermoid), adenocarcinoma, large cell carcinoma (large cell anaplastic), etc.) and small cell lung cancer (oat cell). Non-small cell lung cancer (NSCLC) has different biological properties and responses to chemotherapeutics from those of small cell lung cancer (SCLC). Thus, chemotherapeutic formulas and radiation therapy are different between these two types of lung cancer.

Non-Small Cell Lung Cancer

Where the location of the non-small cell lung cancer tumor can be easily excised (stage I and II disease) surgery is the first line of therapy and offers